

Appendix A

Some embodiments of the present invention describe how to make protein *complexes* between the papillomavirus (PV) L1 and L2 proteins. For example, when the PV L1 protein is recombinantly co-expressed with the L2 protein, *e.g.*, using compatible expression plasmids in bacteria, the L1 protein pentamerizes immediately post-translation and the L2 protein, by virtue of a specific peptide sequence within it, associates with the L1 pentamers forming a *complex* with a final stoichiometry of 5 L1 molecules to one L2 molecule. This L1 interaction amino acid sequence within the L2 protein, which enables the formation of L1+L2 complexes is disclosed in the pending application. In addition, by using this L1 interaction sequence, a complex formed is not restricted, but rather any polypeptide containing the interacting sequence may be used to form a complex with L1. In certain examples, these polypeptides may be termed chimeric, because they contain the L2 interaction sequence recombinantly linked to other protein sequences. Indeed, in the original demonstration of the interacting sequence, a glutathione-S-transferase (GST) protein was linked to L2 in order to observe complex formation of GST-L2 with L1 using glutathione affinity chromatography. No chimeras are claimed for the L1 pentamer, and

the invention is more generally described as a method to form protein complexes between L1 and a second polypeptide, for example, any protein with an L1-interacting sequence.

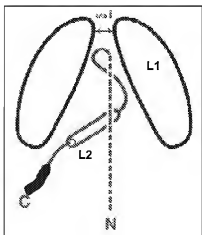


Figure 1. illustrates an exemplary schematic of an L1 pentamer cut away (sliced in half) to illustrate how the L2 interacts with the L1 pentamer in the “donut hole” or five fold axis of interior of the pentamer. The interacting sequence of L2 includes the amino acids of

L2 extending into this concavity, forming contacts with L1. Aside from these interacting amino acids, the remainder of a second polypeptide (*e.g.* L2) may be truncated, modified, or recombinantly linked to other proteins while still maintaining interactions with L1. Because the L1 and L2 are not covalently linked, this structure is a complex of L1 and L2, not a chimeric.